The Need for Linking with Public Health

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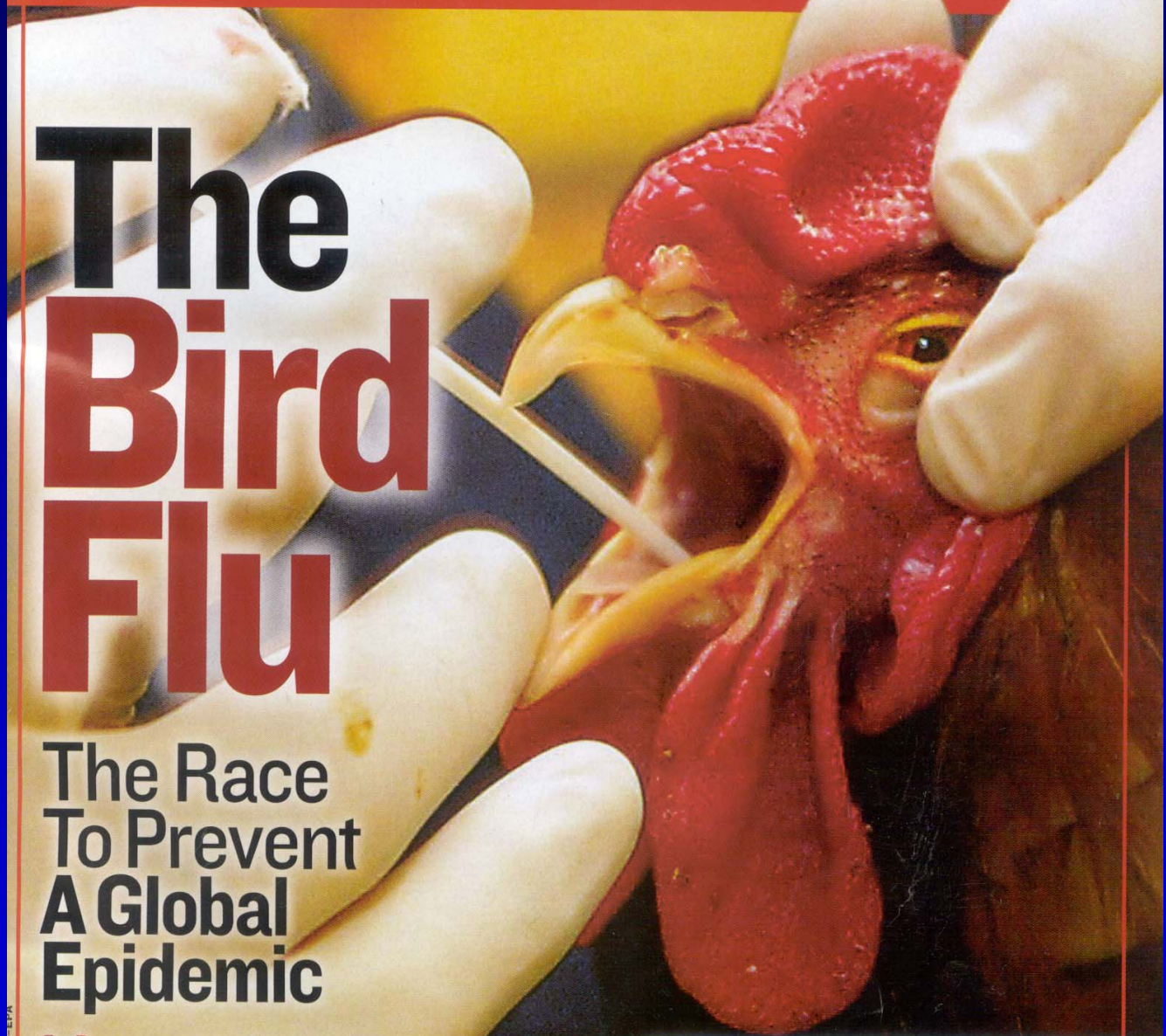
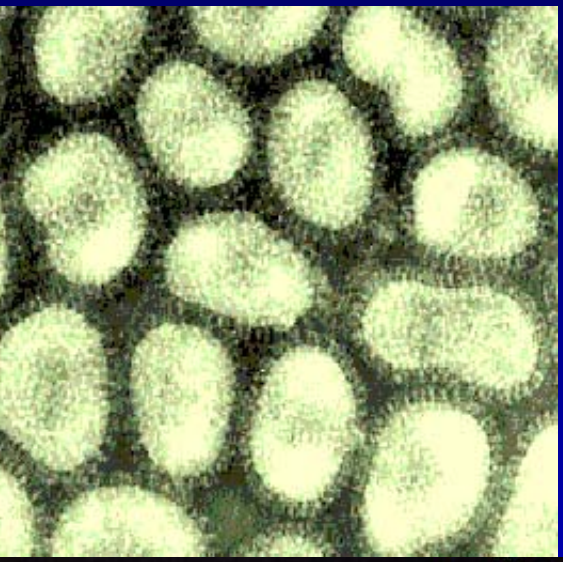
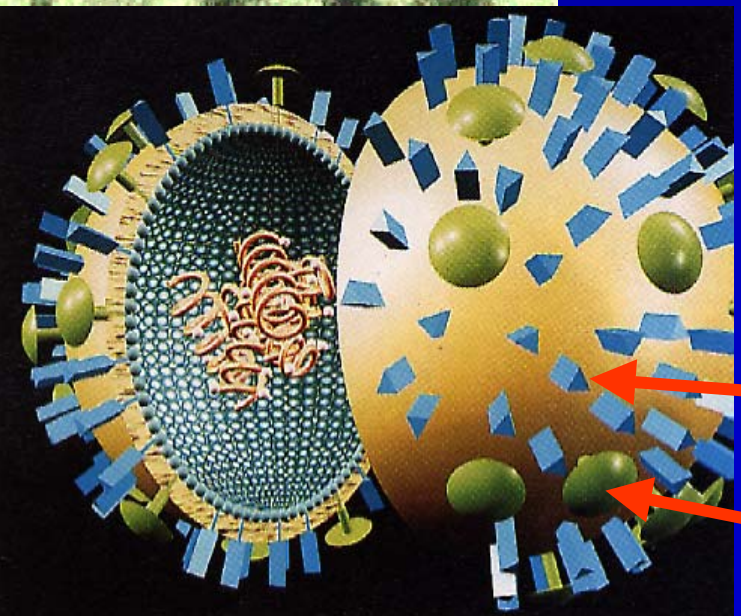


The Bird Flu

The Race To Prevent A Global Epidemic

Key Influenza Viral Features





Surface proteins (major antigens)

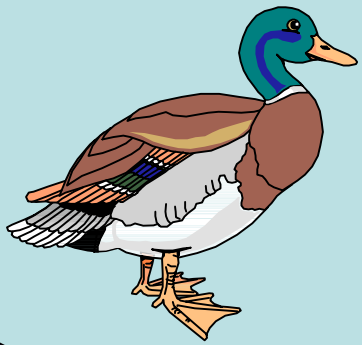
- Hemagglutinin (HA)
  - Site of attachment to host cells
  - *Antibody to HA is protective*
- Neuraminadase (NA)
  - Helps release virions from cells
  - Antibody to NA can help modify disease severity

Natural Reservoir for New Human Influenza A Virus Subtypes: Waterfowl (Aquatic Ducks, Geese)

Avian Influenza A viruses

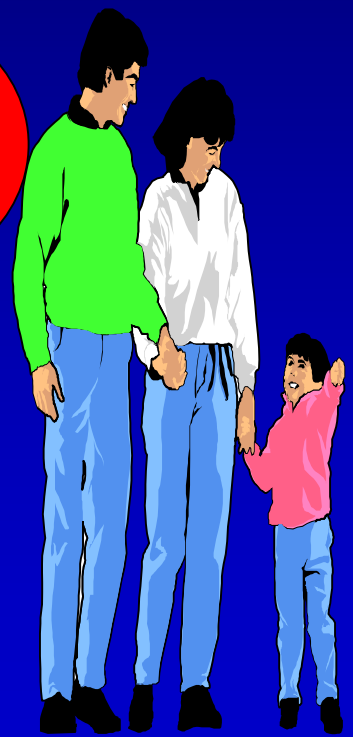
H1 - H16

N1 - N9



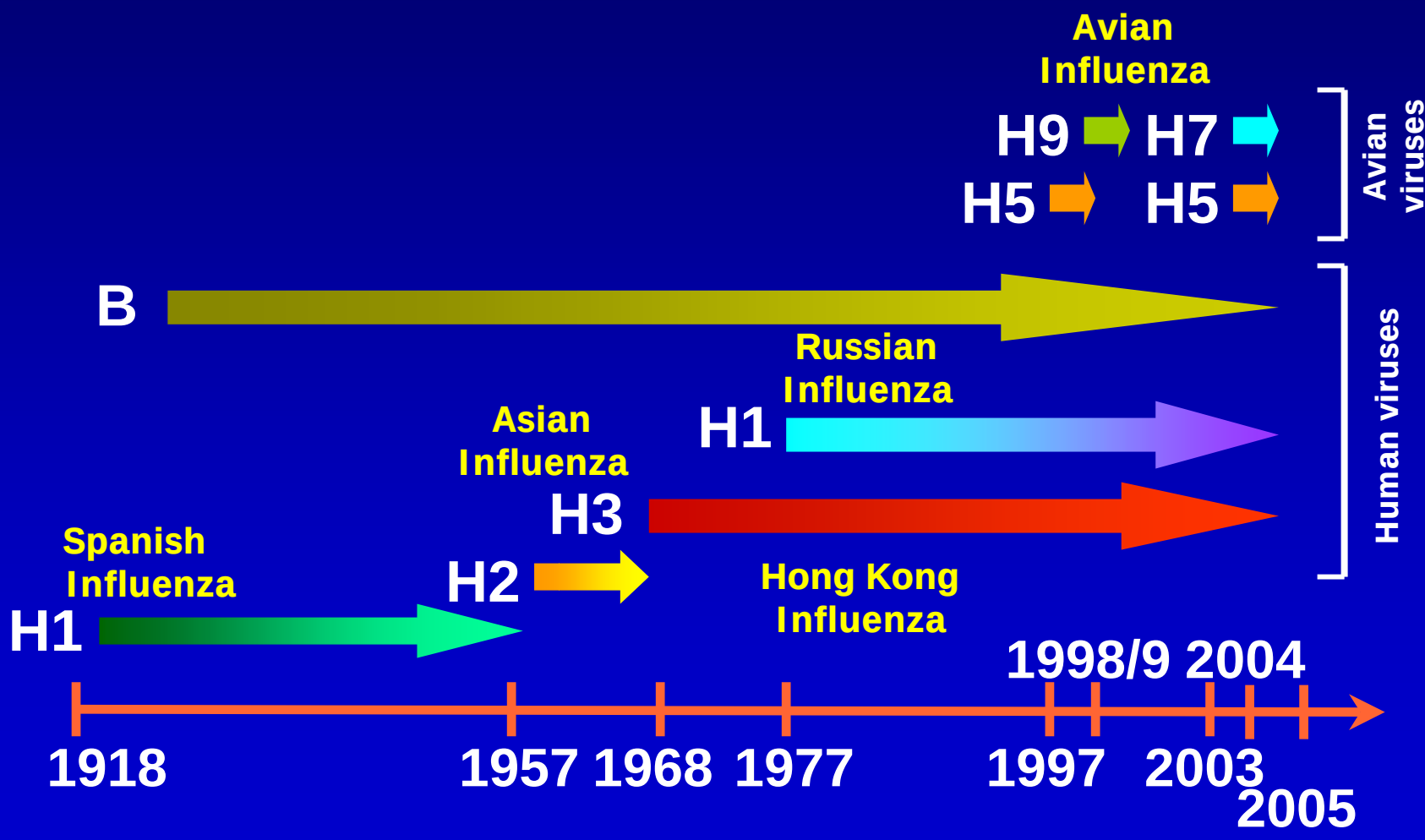
Human Influenza A Viruses

H1 - H3

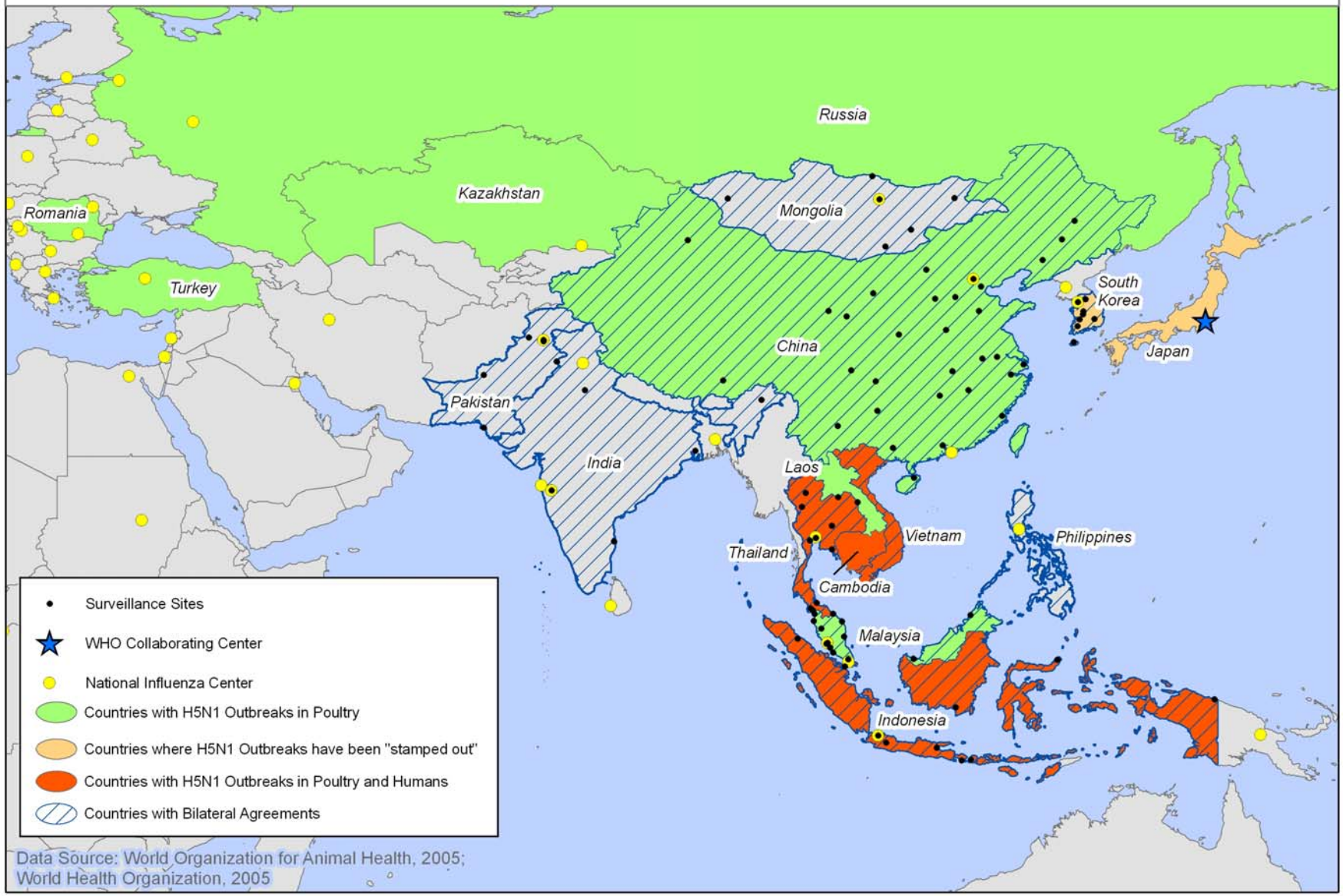


CDC

Timeline of Emergence of Influenza Viruses in Humans



National Influenza Centers, WHO Collaborating Centers, Surveillance Sites, Nations with Bilateral Agreements, Avian Outbreaks, and Human Cases



Human H5N1 Cases, 2004-2005

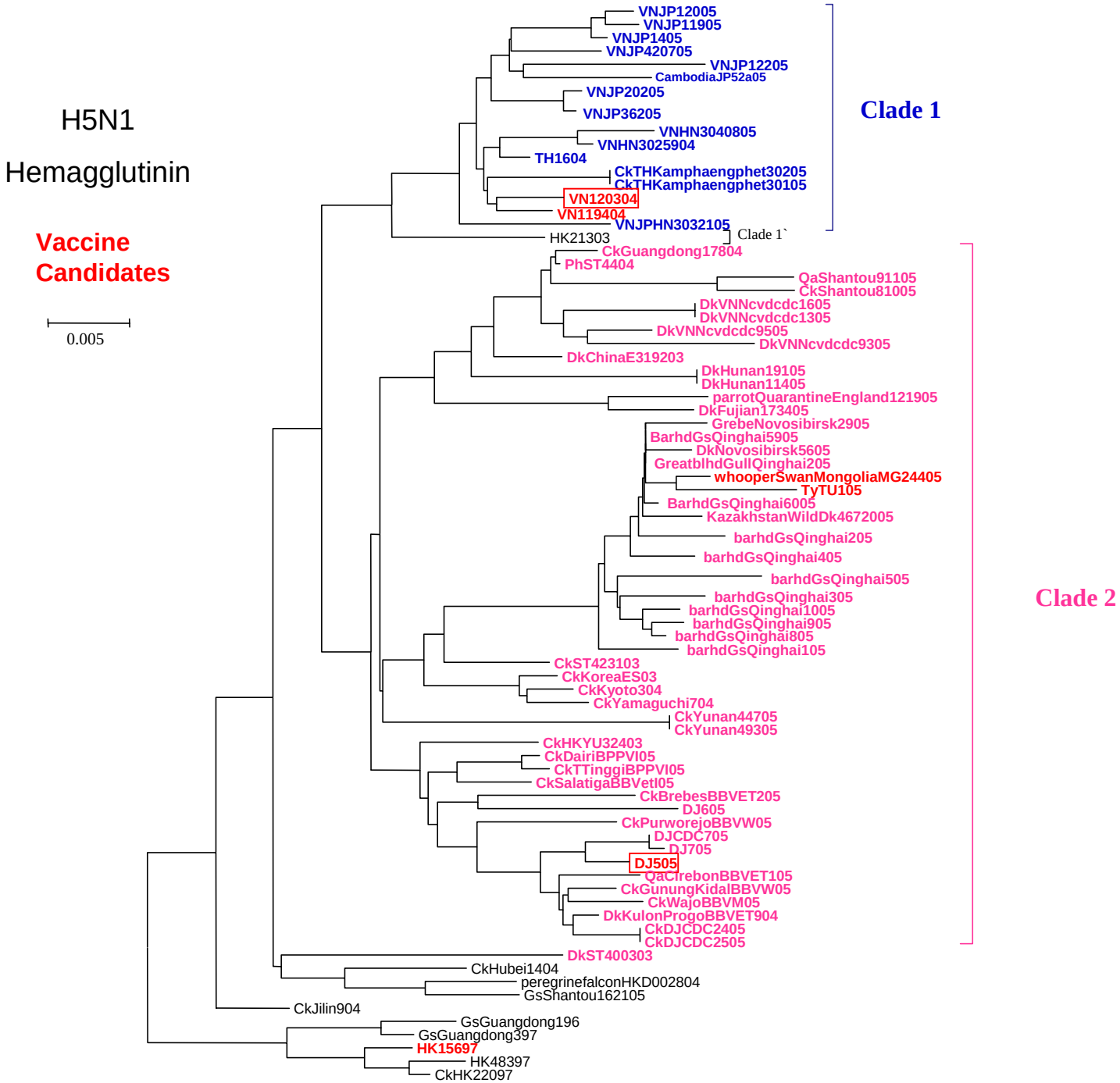
Country	H5N1 Cases	Deaths	Case Fatality
Cambodia	4	4	100%
Indonesia	9	5	55.5%
Thailand	20	13	65%
Vietnam	92	42	45.6%
Total	125	62	51%

- Apparent high case fatality regardless of age
- Clinical symptoms similar to earlier cases, including lymphopenia
- Diarrhea prominent in some cases
- Third wave of infections in Dec. 2004-present
- Thai family cluster; probable H-to-H transmission

CDC

Human H5N1 cases, Asia 2003-05

- **Epidemiology (limited data)**
  - **Median age: @20 years (range: 4 months - 81 years)**
  - **Male: 51%**
  - **Case fatality: 51%**
  - **Most cases: sporadic avian-to-human transmission**
    - **Previously healthy children, young adults in 2004**
    - **Direct contact with sick/dead poultry**
    - **Few cases: consumed uncooked duck blood**
  - **➢ Clustering of cases**
    - **➢ Apparent increase in 2005**
    - **➢ Limited person-to-person H5N1 has occurred**
  - ***➢ No evidence of sustained person-to-person spread***

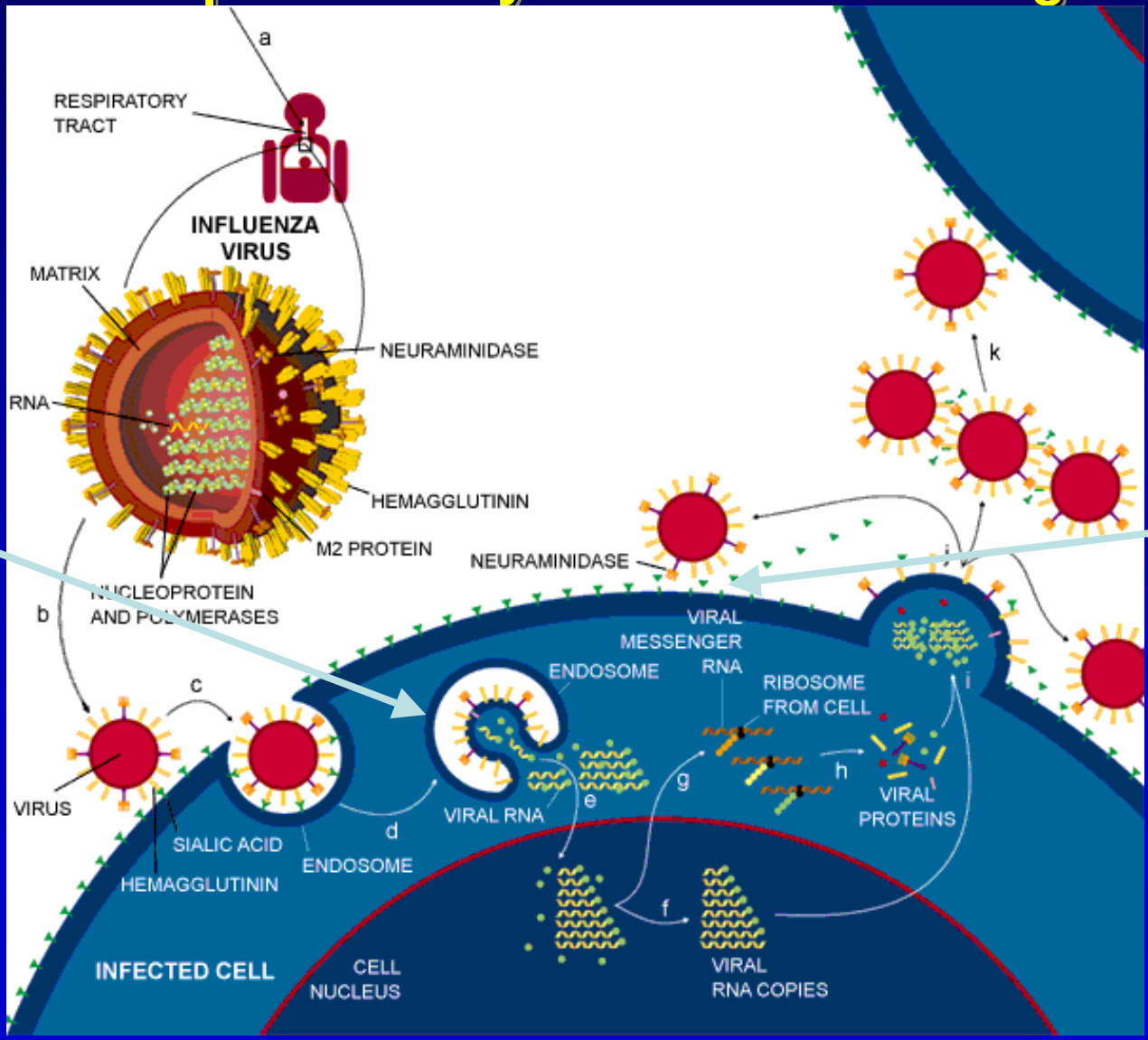

H5N1
Hemagglutinin
Vaccine Candidates
0.005
VNJP12005
VNJP11905
VNJP1405
VNJP420705
VNJP12205
CambodiaJP52a05
VNJP20205
VNJP36205
VNHN3040805
VNHN3025904
TH1604
CkTHKamphaengphet30205
CkTHKamphaengphet30105
VN120304
VN119404
VNJPHN3032105
Clade 1
HK21303
Clade 1`
CkGuangdong17804
PhST4404
QaShantou91105
CkShantou81005
DkVNNcvdcdc1605
DkVNNcvdcdc1305
DkVNNcvdcdc9505
DkVNNcvdcdc9305
DkChinaE319203
DkHunan19105
DkHunan11405
parrotQuarantineEngland121905
DkFujian173405
GrebeNovosibirsk2905
BarhdGsQinghai5905
DkNovosibirsk5605
GreatblhdGullQinghai205
whooperSwanMongoliaMG24405
TyTU105
BarhdGsQinghai6005
KazakhstanWildDk4672005
barhdGsQinghai205
barhdGsQinghai405
barhdGsQinghai505
barhdGsQinghai305
barhdGsQinghai1005
barhdGsQinghai905
barhdGsQinghai805
barhdGsQinghai105
CkST423103
CkKoreaES03
CkKyoto304
CkYamaguchi704
CkYunan44705
CkYunan49305
CkHKYU32403
CkDairiBPPVI05
CkTTinggiBPPVI05
CkSalatigaBBVetI05
CkBrebesBBVET205
DJ605
CkPurworejoBBVW05
DJCDC705
DJ705
DJ505
QaCirebonBBVET105
CkGunungKidalBBVW05
CkWajoBBVM05
DkKulonProgoBBVET904
CkDJCDC2405
CkDJCDC2505
Clade 2
DkST400303
CkHubei1404
peregrinefalconHKD002804
GsShantou162105
CkJilin904
GsGuangdong196
GsGuangdong397
HK15697
HK48397
CkHK22097

HEMAGGLUTINATION INHIBITION REACTIONS OF H5 INFLUENZA SPECIMENS

			REFERENCE ANTISERA					
			A	B	C	D	E	F
REFERENCE ANTIGENS		Date collected	HK/213	VN/1203	HN30408	DK/KP	QU/CIR	IND/5
1	A/HONG KONG/213/2003	2/13/2003	**5120**	320	640	1280	1280	320
2	A/VIETNAM/1203/2004	1/4/2004	10	**160**	320	80	10	20
3	A/VIETNAM/HN30408/05	UNKNOWN	10	160	**320**	80	10	10
4	A/DUCK KULON PROGO/BBVET/1X/04	UNKNOWN	20	20	20	**2560**	1280	640
5	A/QUAIL/CIREBON/BBVET/1/05	UNKNOWN	80	40	20	2560	**1280**	1280
6	A/INDONESIA/5/2005	7/8/2005	20	10	20	1280	640	**640**
TEST ANTIGENS								
1	ISOLATE 1	2/27/2005	10	80	160	80	10	10
2	ISOLATE 2		10	10	20	640	320	320
3	ISOLATE 3		40	10	20	1280	1280	1280
4	ISOLATE 4		40	10	10	2560	2560	1280

H5N1 Treatment

Replication Cycle & Antiviral Drugs



M2 Protein Transmembrane Genotype: Adamantane Resistance

	25	27	31	43		
	....P	L	V	V A A S I I G I L H L I L W I	L.....	
Vn/1203/04				N	Human	Amantadine Resistant
Vn/1194/04				N		
Vn/3212/04				N		
Thai/16/04				N		
Thai/sp83/04				N		
DJ/7CDC/05		A		S		
Ck/Vn/NCVD11/03				N		
Ck/Laos/7192/04				N	Avian	
CK/DJ/24/2005		A		S		
Dk/VN/NCVD4/03				S	Avian	
Dk/Vn/NCVD9/03				S		
Dk/Vn/NCVD25/03				S		
Ck/S.Korea/ES/03				S		
Gs/VN/113/01				S		

H5N1 Human Vaccine Issues

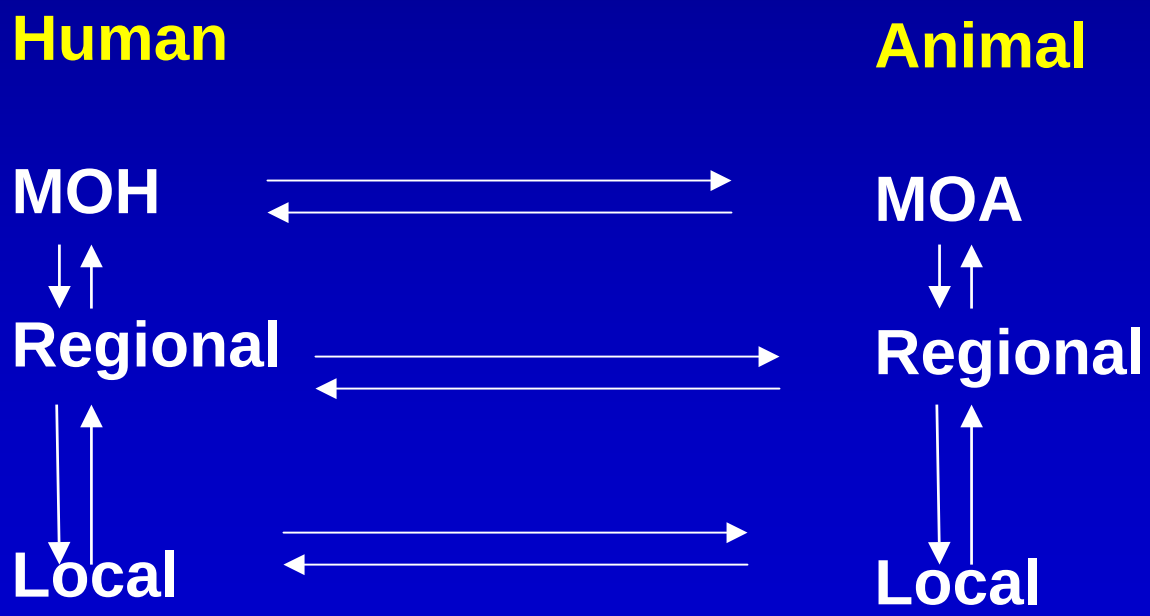
- No currently available human H5N1 vaccine
- Human clinical trials of an inactivated H5N1 vaccine in-progress in the U.S.
  - Phase I and II clinical trials (NIH sponsored)
  - 3 sites (U. Rochester, U. Maryland, UCLA)
  - Participants: 450 healthy adults aged 18-64 years
  - Elderly and children to be enrolled later
- Other countries planning adjuvanted vaccines
- Vietnam developed an inactivated H5N1 vaccine
  - Animal trials in-progress
  - Human clinical trials planned

The need for linking with public health

Work closely with animal health authorities

. Reduce risk of exposure to infected poultry/animals

.Active surveillance for H5N1 viruses in poultry and humans



The need for linking with public health

- Surveillance for severe respiratory illness
- Actively investigate cases, especially clusters
  - Assess potential for person-to-person transmission
  - Identify possible poultry exposures
  - Surveillance of known contacts
- Isolate cases
  - Antiviral treatment (oseltamivir) for cases, supportive care
  - Collect respiratory specimens for H5N1 testing (RT-PCR)
- Protect HCWers:
  - PPE, antiviral chemoprophylaxis, human influenza vaccine
- Protect AWers:
  - Reduce risk of exposure to infected poultry/animals
    - Active surveillance for H5N1 viruses in poultry
    - Depopulation of infected poultry (using PPE)
    - Environmental decontamination
    - Poultry vaccination to reduce viral burden in poultry

Conclusions

- Avian influenza viruses pose a major risk to global public health
- Early detection H-2-H transmission is essential
- 2003/05 Asian H5N1 viruses are heterogeneous in antigenicity, AV susceptibility and pathogenicity
- Need for ongoing vaccine development, antiviral stockpiling and pandemic preparedness
- Surveillance in animals is critical
- Information and specimen exchange between human and veterinary health authorities essential
- Research agenda needed to enhance our understanding of the genesis of pandemics

H5N1 Treatment

- Supportive care
- Broad-spectrum antibiotics to cover secondary bacterial infections
- Antiviral therapy: Most H5N1 viruses are resistant to amantadine and rimantadine
- Most H5N1 viruses are sensitive to oseltamivir and zanamivir: one H5N1 virus was resistant to oseltamivir
- Role of corticosteroids is controversial